

Application No.: 10/740,264

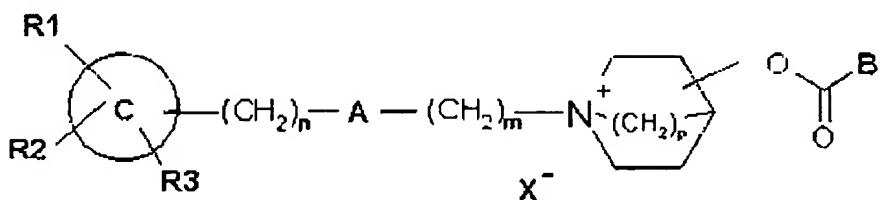
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AMENDMENTS TO THE CLAIMS

Claims 1-35 (cancelled)

Claim 36 (previously presented): A compound according to formula (I)



(I)

wherein:

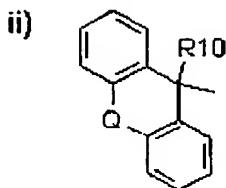
- © is a phenyl ring, a C₄ to C₉ heteroaromatic group containing one or more heteroatoms or a naphthalenyl, 5,6,7,8-tetrahydronaphthalenyl or biphenyl group;
- R¹, R² and R³ each independently represent a hydrogen atom or halogen atom, or a hydroxy group, or a phenyl, -OR⁴, -SR⁴, -NR⁴R⁵, -NHCOR⁴, -CONR⁴R⁵, -CN, -NO₂, -COOR⁴ or -CF₃ group, or a straight or branched lower alkyl group which may optionally be substituted with a hydroxy or alkoxy group, wherein R⁴ and R⁵ each independently represent a hydrogen atom, straight or branched lower alkyl group or together form an alicyclic ring; or R¹ and R² together form an aromatic, alicyclic or heterocyclic ring,
- n is an integer from 0 to 4;
- A represents a -CH₂- , -CH=CR⁶- , -CR⁶=CH- , -CR⁶R⁷- , -CO-, -O-, -S-, -S(O)-, SO₂ or -NR⁶- group, wherein R⁶ and R⁷ each independently represent a hydrogen atom, straight or branched lower alkyl group or R⁶ and R⁷ together form an alicyclic ring;
- m is an integer from 0 to 8; provided that when m = 0, A is not -CH₂-;
- p is an integer from 1 to 2 and the substitution in the azoniabicyclic ring may be in the 2, 3 or 4 position including all possible configurations of the asymmetric carbons;
- B represents a group of formula ii):

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wherein R¹⁰ represents a hydrogen atom, a hydroxy or methyl group; and Q represents a single bond, -CH₂-, -CH₂-CH₂-, -O-, -O-CH₂-, -S-, -S-CH₂- or -CH=CH-; and X represents a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 37 (previously presented): A compound according to claim 36, wherein any alkyl group present as R¹ to R⁷ contains from 1 to 4 carbon atoms.

Claim 38 (previously presented): A compound according to claim 36 wherein p=2.

Claim 39 (previously presented): A compound according to claim 36 wherein © represents a phenyl, pyrrolyl, thienyl, furyl, biphenyl, naphthalenyl, 5,6,7,8-tetrahydronaphthalenyl, benzo[1,3]dioxolyl, imidazolyl or benzothiazolyl group.

Claim 40 (previously presented): A compound according to claim 39, wherein © represents a phenyl, pyrrolyl or thienyl group.

Claim 41 (previously presented): A compound according to claim 36 wherein R¹, R² and R³ each independently represent a hydrogen or halogen atom or a hydroxy, methyl, tert-butyl, -CH₂OH, 3-hydroxypropyl, -OMe, -NMe₂, -NHCOMe, -CONH₂, -CN, -NO₂, -COOMe or -CF₃ group.

Claim 42 (previously presented): A compound according to claim 41 wherein R¹, R² and R³ each independently represent a hydrogen or halogen atom or a hydroxy group.

Claim 43 (previously presented): A compound according to claim 42, wherein the halogen atom is fluorine.

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Claim 44 (previously presented): A compound according claim 36 wherein A represents a -CH₂-, -CH=CH-, -CO-, -NH-, -NMe-, -O- or -S- group; n is 0 or 1; and m is an integer from 1 to 6.

Claim 45 (previously presented): A compound according to claim 44, wherein A represents a -CH₂-, -CH=CH- or -O- group and m is 1, 2 or 3.

Claim 46 (previously presented): A compound according claim 36 wherein the azoniabicyclo group is substituted on the nitrogen atom with a 3-phenoxypropyl, 2-phenoxyethyl, 3-phenylallyl, phenethyl, 3-phenylpropyl, 4-phenylbutyl, 3-(2-hydroxyphenoxy)propyl, 3-(4-fluorophenoxy)propyl, 2-benzyloxyethyl, 3-pyrrrol-1-ylpropyl, 2-thien-2-ylethyl or 3-thien-2-ylpropyl group.

Claim 47 (previously presented): A compound according claim 36, wherein Q represents a single bond, a -CH₂-, -CH₂-CH₂- group or an oxygen atom.

Claim 48 (previously presented): A compound according claim 36 wherein X represents a bromide, chloride or trifluoroacetate anion.

Claim 49 (previously presented): A compound according to claim 36 wherein the azoniabicyclo group is substituted in the 3-position.

Claim 50 (previously presented): A compound according to claim 49, wherein the substituent in the 3 position has (R) configuration.

Claim 51 (previously presented): A compound according to claim 36 which is a single stereoisomer.

Claim 52 (previously presented): A compound according to claim 36 which is 1-(3-phenylallyl)-3(R)-(9-Hydroxy-9[H]-fluorene-9-carbonyloxy)-1-azoniabicyclo[2.2.2]octane; bromide

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3(R)-(9-Hydroxy-9[H]-fluorene-9-carbonyloxy)-1-(3-phenoxypropyl)-1-azoniabicyclo

[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9[H]-fluorene-9-carbonyloxy)-1-phenethyl-1-

azoniabicyclo[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9H-fluorene-9-carbonyloxy)-1-(3-thien-2-ylpropyl)-1-azoniabicyclo

[2.2.2]octane; bromide

3(R)-(9-Methyl-9[H]-fluorene-9-carbonyloxy)-1-(3-phenylallyl)-1-

azoniabicyclo[2.2.2]octane; bromide

3(R)-(9-Methyl-9[H]-fluorene-9-carbonyloxy)-1-(3-phenoxypropyl)-1-azoniabicyclo

[2.2.2]octane; bromide

1-(4-Phenylbutyl)-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-

azoniabicyclo[2.2.2]octane; bromide

1-(2-Phenoxyethyl)-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-

azoniabicyclo[2.2.2]octane; bromide

1-(3-Phenoxypropyl)-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-

azoniabicyclo[2.2.2]octane; bromide

1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo

[2.2.2] octane; bromide

3(R)-(9-Hydroxy-9[H]-xanthene-9-carbonyloxy)-1-(3-phenoxypropyl)-1- azoniabicyclo

[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9[H]-xanthene-9-carbonyloxy)-1-phenethyl-1-

azoniabicyclo[2.2.2]octane; bromide

3(R)-(9-Hydroxy-9H-xanthene-9-carbonyloxy)-1-(3-thien-2-ylpropyl)-1-azoniabicyclo

[2.2.2]octane; bromide or

3(R)-(9-Methyl-9[H]-xanthene-9-carbonyloxy)-1-(3-phenoxy-propyl)-1-azoniabicyclo

[2.2.2]octane; bromide.

Claim 53 (previously presented): A compound according to claim 36, wherein it has an IC₅₀ value for muscarinic M₃ receptors (Hm3) of less than 35 nM.

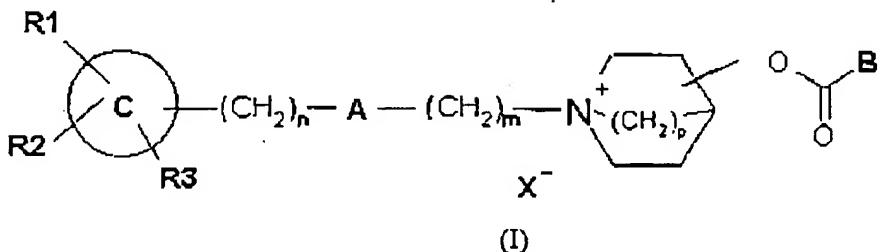
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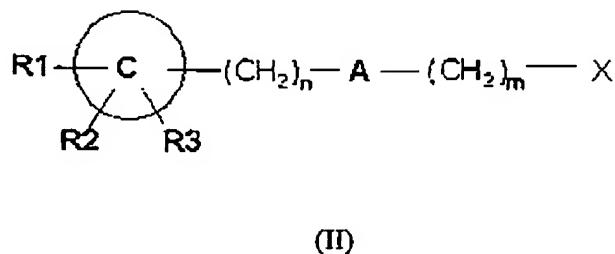
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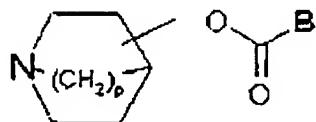
Claim 54 (previously presented): A process for the preparation of a compound of formula (I)



which comprises reacting an alkylating agent of formula (II)



with a compound of formula (III)



(III)

to obtain a reaction mixture comprising the compound of formula (I), wherein, in each of formulae I, II and III, R^1 , R^2 , R^3 , C , A , X , B , n , m and p are as defined in claim 36.

Claim 55 (previously presented): A process according to claim 54, wherein the reaction mixture is purified by solid phase extraction.

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Claim 56- 60 (cancelled)

Claim 61 (previously presented): A pharmaceutical composition comprising a compound according to claim 36 in admixture with a pharmaceutically acceptable carrier or diluent.

Claim 62 (cancelled).

Claim 63 (currently amended): A method for treating COPD, chronic bronchitis, bronchial hyperreactivity, asthma and/or rhinitis which method comprises administering to a human or animal patient in need of such treatment an effective amount of a compound according to any one of claims 36-53 or of a pharmaceutical composition according to claim 61.

Claim 64 (new): A pharmaceutical composition according to claim 61, wherein the pharmaceutically acceptable carrier or diluent is aqueous.

Claim 65 (new): A compound according to claim 36, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X-, wherein X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 66 (new): A compound according to claim 65, wherein X- is Br-.

Claim 67 (new): A pharmaceutical composition according to claim 61 or 64, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X-, wherein X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 68 (new): A pharmaceutical composition according to claim 67 wherein X- is Br-.

Claim 69 (new): A method for treating COPD, chronic bronchitis, bronchial hyperreactivity, asthma and/or rhinitis which method comprises administering to a human or animal

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patient in need of such treatment an effective amount of 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X-, or

administering to a human or animal patient in need of such treatment an effective amount of a pharmaceutical composition comprising 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X-, and wherein:

X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 70 (new): A method according to claim 69, wherein X- is Br-.

Claim 71 (new): A pharmaceutical composition prepared by mixing a compound according to claim 36 with a pharmaceutically acceptable carrier or diluent.

Claim 72 (new): A pharmaceutical composition according to claim 71, wherein the pharmaceutically acceptable carrier or diluent is aqueous.

Claim 73 (new): A pharmaceutical composition according to claim 71 or 72, wherein the compound is 1-Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X-, and wherein:

X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.

Claim 74 (new): A pharmaceutical composition according to claim 73, wherein X- is Br-.

Claim 75 (new): A method for treating COPD, chronic bronchitis, bronchial hyperreactivity, asthma and/or rhinitis, which method comprises administering to a human or animal patient in need of such treatment an effective amount of a pharmaceutical composition according to claim 71.

Claim 76 (new): A method according to claim 75, wherein the pharmaceutically acceptable carrier or diluent is aqueous.

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**Claim 77 (new): A method according to claim 75 or 76, wherein the compound is 1-
Phenethyl-3(R)-(9[H]-xanthene-9-carbonyloxy)-1-azoniabicyclo [2.2.2] octane; X-, and wherein:
X- is a pharmaceutically acceptable anion of a mono or polyvalent acid.**

Claim 78 (new): A method according to claim 77, wherein X- is Br-.

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